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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,800	03/13/2006	Chaim M. Roifman		4283

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EXAMINER	
FINN, MEGHAN R	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,800	ROIFMAN ET AL.	
	Examiner	Art Unit	
	MEGHAN FINN	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,7,8,12-16,57-60 and 69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,7,8,12-16,57-60 and 69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's Amendment filed January 15, 2009 has been received and entered into present application. No claims were canceled or added, thus claims 1, 4, 7-8, 12-16, 57-60, and 69 are pending.

Applicants' arguments, filed January 15, 2009, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1, 4, 7-8, 12-16, 57-60, and 69 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In claims 1, 4, and 8, applicant claims a method of treating with the compounds of formula I, with an elected species of CR4, and "salt, solvate, or hydrate thereof".

While the salt form of a compound is a well known and accepted modification to a compound, solvates are not. The examiner has noted that applicant has argued against and deleted the word "prodrug" from the claims, which renders moot that particular point of the previous written description rejection, but applicant has not addressed solvates and how one of skill in the art would be able to determine, from the direction provided by applicant what compounds are considered solvates. Thus the rejection of claims 1, 4, 7-8, 12-16, 57-60, and 69 is **maintained.**

Claims 57-60 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibiting secretion of vascular endothelial growth factor, does not reasonably provide enablement for treating those who are at risk for developing tumors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicant has established enablement for treatment of breast cancer and inhibiting VEGF secretion, and thus the enablement rejection for those claims has been withdrawn. However, for claims 57-60, which claim a method of treating an animal is "*at risk of* developing, a vascularized solid tumor, a metastatic tumor or metastases from a primary tumor", this rejection is maintained because applicant has not enabled treatment of animals who are at risk (i.e., prevention). Applicant has argued that that one of skill in the art would know who is at risk for developing these tumors, and has submitted information on risk factors for various types of cancers. However, while some

groups have been identified as being at risk, it is by no means known in the art everyone who is at risk, and cancer is especially unpredictable and can be caused by external factors which are not appreciated. Furthermore, it is noted that claims 57-60 are not limited to any particular type of cancer, only to patients in need of inhibiting secretion of VEGF and at risk for developing a vascularized solid tumor or a metastatic tumor, and is thus incredibly broad. One of skill in the art would not be able to determine who is at risk for any of these tumors and therefore cannot use the invention as claimed.

Applicant's arguments were carefully considered but are not deemed persuasive and thus the rejection of claims 57-60 is **maintained.**

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 8, 12-16, 57-60 and 69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roifman et al. (WO 01/79158 A2, cited on applicant's IDS) in view of Bessette et al. (US 2003/0017215 A1) in further view of Butler et al. (US 5,486,457), each already of record, for the reasons set forth at pages 6-8 of previous office action dated July 15, 2008, of which reasons are herein incorporated by reference.

Claims 8, 12-16, 57-60 and 69 were rejected in the previous office action and applicant's amendment to the claims to remove prodrug does not change this prior art rejection. Applicant has argued that none of the prior art teaches inhibition of VEGF secretion and that applicant has an "unexpected discovery" that certain compounds are capable of inhibiting the activity of VEGF. While this argument applies to claims 1, 4, and 7, claims 8, 12-16, 57-60 and 69 are directed towards treating a disorder caused by VEGF, of which breast cancer is the preferred disorder (claims 8, 12-16), and inhibiting VEGF secretion in a animal that has a vascularized solid tumor of a metastatic tumor (claims 57-60) or a method of interfering with angiogenesis in a mammal having a condition characterized by angiogenesis (claim 69). For claims 8, 12-16, as discussed previously it would be obvious to use the compounds of Roifman et al. to treat cancer in general and it would be obvious to use them to treat breast cancer in light of the teachings of Bessette et al. and Butler et al. The method taught by the prior art of treating breast cancer with the compounds is treating the same patients with the same

composition and would necessarily have the same results even if the prior art does not mention that breast cancer is a disorder that is caused or contributed to by VEGF. For claims 57-60, Roifman et al. teaches treatment of cancer in general and the patients in claims 57-60 having solid vascularized tumors would be obvious to treat with the compounds of Roifman et al., as discussed in the previous office action. And for claim 69, it would have been obvious to one of ordinary skill in the art at the time of the invention that angiogenesis is involved in most cancers, including breast cancer and therefore would also be obvious over Roifman et al. in view of Bessette et al. and Butler et al.

This argument is not deemed persuasive and thus the rejection of claims 8, 12-16, 57-60 and 69 is **maintained.**

New rejection under 35 USC § 103

Claims 1, 4, 7-8, 12-16, 57-60, and 69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roifman et al. (WO 01/79158 A2, cited on applicant's IDS) in view of Foekens et al. (Cancer Research, 2001, Vol. 61, Pages 5407-5414).

In claim 1, applicant claims a method of inhibiting secretion of vascular growth factor in an animal in need of such treatment comprising administering the elected species, CR4. In claim 4 applicant claims a method of inhibiting an effect of VEGF in an animal in need of such inhibition. Roifman et al. teaches treatment of cancer (abstract) and specifically teaches CR4 (page 19, line 1 and figures 1-7, page 6). They also teach that these compounds can be used to inhibit proliferation in a cancer cell, any type of

cancer (page 5, lines 6-15). It would be obvious to one of ordinary skill in the art at the time of the invention that breast cancer is a type of cancer and that cell proliferation occurs in breast cancer. Foekens et al. teaches that in patients with breast cancer VEGF levels have been found to be elevated (page 5407, column 2). Thus it would have been obvious to one of ordinary skill in the art at the time of the invention to use the compounds of Roifman et al. to treat breast cancer and that patients with breast cancer are in need of inhibiting secretion of VEGF. Thus the prior art teaches treatment of the same patients with the same compounds, and while applicant has made an significant scientific discovery that VEGF is involved in the mechanism of action in the compounds of Roifman et al., it is not a patentable distinction as the same method of treatment is already suggested and motivated in the prior art. Thus claims 1 and 4 are unpatentable over Roifman et al. in view of Foekens et al.

In claim 7, applicant claims the effect of VEGF is angiogenesis. Roifman et al. teaches treatment of cancer and it would have been obvious to one of ordinary skill in the art at the time of the invention that a cancer patient is in need inhibition of angiogenesis, and angiogenesis as a part of cancer is taught by Foekens et al. (page 5407, column 1) and thus for the reasons discussed above claim 7 is unpatentable over Roifman et al. in view of Foekens et al.

In claim 8, applicant claims a method of treating a disorder caused by or contributed by VEGF. In claims 13-15 applicant claims that the disorder is cancer, specifically breast cancer. As discussed above, Roifman et al. teaches treatment of all cancers with the elected species and Foekens et al. teaches that breast cancer is a

cancer in which VEGF levels are elevated, thus it is disorder that is contributed to by VEGF and claim 8 and claims 13-15 are unpatentable over Roifman et al. in view of Foekens et al.

In claim 12, applicant claims the method of claim 8, wherein expression levels of VEGF are upregulated in the disorder. This is claiming a characteristic of a disorder, since treatment of the disorder with those compounds is taught by the prior art, the characteristic necessarily flows from the disorder and is thus encompassed by the treatment of cancer taught by the prior art. Thus claim 12 is unpatentable over Roifman et al. in view of Foekens et al.

In claim 16, applicant claims the growth of the tumor is inhibited. This is a characteristic of the treatment, thus the same treatment to the same patients would result in this inhibition. Additionally, Roifman et al. teaches that CR4 reduced tumors (page 27, lines 26-31). Thus claim 16 is unpatentable over Roifman et al. in view of Foekens et al.

In claims 57-60 applicant claims the animal has a tumor which as discussed above is obvious as Roifman et al. teaches treatment of cancer and tumors, and that the treatment is combined with at least a second anti-cancer agent which is taxol. As discussed in the previous office action, taxol is well known for the treatment of cancer and it is obvious to combine to drugs known for treating the same disorder and thus it would have been obvious to one or ordinary skill in the art at the time of the invention to use the compounds of Roifman et al. in combination with taxol. Thus claims 57-60 are unpatentable over Roifman et al. in view of Foekens et al.

In claim 69, applicant claims a method of interfering with angiogenesis in a mammal having a condition characterized by angiogenesis. Cancer is such a condition, as taught by Foekens et al. and thus claim 69 is also unpatentable over Roifman et al. in view of Foekens et al.

Conclusion

No claims are allowed.

This rejection is non-final because of the new rejection over Roifman et al. in view of Foekens et al. that was not necessitated by amendment to the claims.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Meghan Finn whose telephone number is (571) 270-3281. The examiner can normally be reached on 9:30am-7pm Mon-Thu, 9:30am-6pm Friday (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Meghan Finn

/James D Anderson/
Examiner, Art Unit 1614